09/898,574
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#9
attachment

(FILE 'HOME' ENTERED AT 13:41:49 ON 19 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:41:57 ON 19 MAR 2003

L1 168 S MANNOSE (3N) DEHYDRATASE
L2 21 S L1 AND LEUKOCYTE AND ADHESION AND DEFICIENCY
L3 7 DUP REM L2 (14 DUPLICATES REMOVED)
L4 1707 S LEUKOCYTE AND ADHESION AND DEFICIENCY
L5 22 S L4 AND DEHYDRATASE
L6 8 DUP REM L5 (14 DUPLICATES REMOVED)
L7 12990 S DEHYDRATASE
L8 253 S L7 AND (ARTHRITIS OR ASTHMA OR SEPSIS OR REPERFUSION OR STRO
L9 181 DUP REM L8 (72 DUPLICATES REMOVED)
L10 16 S L9 AND FUCOSE

FILE 'STNGUIDE' ENTERED AT 13:45:52 ON 19 MAR 2003
L11 0 S FUCOSE AND (ARTHRITIS OR ASTHMA OR SEPSIS OR REPERFUSION OR S

FILE 'MEDLINE, CAPLUS, BIOSIS, AGRICOLA' ENTERED AT 13:53:10 ON 19 MAR 2003
L12 1592 S FUCOSE AND (ARTHRITIS OR ASTHMA OR SEPSIS OR REPERFUSION OR S
L13 406 S L12 AND METABOLISM
L14 119 S L13 AND MANNOSE
L15 99 DUP REM L14 (20 DUPLICATES REMOVED)
L16 16 S L15 AND INHIBITOR
L17 28 S L15 AND (INHIBITOR OR ANTIBODY OR MODULATOR)
L18 28 DUP REM L17 (0 DUPLICATES REMOVED)
L19 480 S FUCOSE AND (LEUKOCYTE)
L20 144 S L19 AND METABOLISM
L21 123 DUP REM L20 (21 DUPLICATES REMOVED)
L22 30 S L21 AND MANNOSE
L23 458 S FUCOSE AND (INFLAM?)
L24 125 S L23 AND METABOLISM
L25 38 S L24 AND (MODULATOR OR ANTIBODY OR INHIBITOR)
L26 34 DUP REM L25 (4 DUPLICATES REMOVED)

	Type	Hits	Search Text	DBs
1	BRS	38	gdp near5 mannose near5 dehydratase	USPAT; US-PGPUB; EPO; JPO; DERWENT;
2	BRS	38	gdp near5 mannose near5 dehydratase	USPAT; US-PGPUB; EPO; JPO; DERWENT;
3	BRS	27	(gdp near5 mannose near5 dehydratase) and (disease)	USPAT; US-PGPUB; EPO; JPO; DERWENT;
4	BRS	35	(gdp near5 mannose near5 dehydratase) and (disease or treatment or stroke or infection or arthritis)	USPAT; US-PGPUB; EPO; JPO; DERWENT;
5	BRS	3	GDP near5 fucose near4 metabolism	USPAT; US-PGPUB; EPO; JPO; DERWENT;
6	BRS	38	GDP near3 mannose near3 dehydratase	USPAT; US-PGPUB; EPO; JPO; DERWENT;
7	BRS	34	l1 and (aberrant or disease or inhibitor or modulator or modulate or inhibit or defective or disease or inflammatory)	USPAT; US-PGPUB; EPO; JPO; DERWENT;
8	BRS	38	gdp near5 mannose near5 dehydratase	USPAT; US-PGPUB; EPO; JPO; DERWENT;

L4 ANSWER 20 OF 20 MEDLINE DUPLICATE 10
AN 86081779 MEDLINE
DN 86081779 PubMed ID: 4076184
TI Purification and characterization of **GDP**-D-**mannose** 4,6-**dehydratase** from porcine thyroid.
AU Broschat K O; Chang S; Serif G
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1985 Dec 2) 153 (2) 397-401. Journal code: 0107600. ISSN: 0014-2956.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198601
ED Entered STN: 19900321
Last Updated on STN: 19970203
Entered Medline: 19860130
AB The enzyme **GDP**-D-**mannose** 4,6-**dehydratase** has been purified 1500-fold from porcine thyroid tissue. The enzyme exhibits a molecular mass of 251000 Da as determined by sedimentation techniques. Its subunit size was determined as 41500 Da by dodecyl sulfate gel electrophoresis. The enzyme has a Km of 3.3 microM with respect to GDP-D-mannose and appears specific with respect to this substrate. The enzyme appears to be **inhibited** by guanine nucleotides and by guanine nucleotide sugars. It is particularly susceptible to **inhibition** by GDP-L-fucose. It is suggested that this compound may have a physiological function as an end-product feedback **inhibitor**.

ANSWER 30 OF 30 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1993:200534 BIOSIS
DN PREV199344096784
TI **Leukocyte** adhesion deficiency (LAD II): Deficiency in sialyl Lewis X, a ligand for selectin: Due to general **fucose** deficiency.
AU Etzioni, Amos (1); Harlan, John M.; Philipps, M. Laurie; Pollack, Shimon; Gershoni-Baruch, Ruth; Paulson, James C.
CS (1) Rambam Med. Center, Haifa Israel
SO Journal of Cellular Biochemistry Supplement, (1993) Vol. 0, No. 17 PART A, pp. 326.
Meeting Info.: Keystone Symposium on Cell Adhesion Mechanisms in Leukocyte Traffic Keystone, Colorado, USA January 24-31, 1993
ISSN: 0733-1959.
DT Conference
LA English

ANSWER 40 OF 43 CAPLUS COPYRIGHT 2003 ACS

AN 1998:336544 CAPLUS

DN 129:94515

TI Use of high molecular weight **fusion** tags to purify **recombinant** proteins by ultrafiltration and affinity chromatography

AU Sakhamuru, K.; Chaudhuri, J. B.; Hough, D. W.

CS Department of Chemical Engineering, University of Bath, UK

SO IChemE Research Event, A Two-Day Symposium, Newcastle upon Tyne, Apr. 7-8, 1998 (1998)., 1375-1383 Publisher: Institution of Chemical Engineers, Rugby, UK.
CODEN: 65ZTAL

DT Conference

LA English

AB The construction of **fusion** proteins has facilitated highly selective purifn. of **recombinant** proteins. Modification with a polypeptide tag has enabled recovery of these products by affinity chromatog. Purifn. of **fusion** proteins, however, need not be tackled via the chromatog. route; we have constructed a **fusion** protein in order to purify it on the basis of mol. wt. using ultrafiltration membranes. The model protein is the enzyme **glucose dehydrogenase** with a .beta.-galactosidase **fusion** tag. On cloning in Escherichia coli, this **fusion** protein is produced intracellularly and hence requires several downstream processing steps to obtain pure target protein. Using the ultrafiltration or affinity approach to recover the **fusion** reduces the no. of steps when compared to non-**fusion** protein purifn. In addn. fractionation by ultrafiltration could result in high yield and purity comparable to affinity sepn., but with reduced costs. The **fusion** protein was constructed with an enzyme specific cleavage site in order to remove the .beta.-galactosidase tag. Cleavage takes place after recovery of **fusion** protein leaving a final **glucose dehydrogenase** purifn.

-continued

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: oligoucleotide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CAGAAAGTCC ACTTCAGTCG GTCGGTAGTA 30

What is claimed is:

1. A composition comprising an antibody which binds to

(a) the amino acid sequence of SEQ ID NO: 2;

(b) the amino acid sequence of SEQ ID NO: 3; and

(c) a fragment of the amino acid sequence of (a) or (b) having GDP-D-mannose 4,6-dehydratase activity; said peptide being substantially free from association with other proteins.

* * * * *

-continued

(i i) MOLECULE TYPE: oligonucleotide

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CAGAAAGTCC ACTTCAGTCG GTCGGTAGTA 30

What is claimed is:

1. An isolated polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence of SEQ ID NO:1;

(b) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:2;

(c) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:3;

(d) a nucleotide sequence encoding a fragment of the amino acid sequence of (b) or (c) having GDP-mannose, 4,6 dehydratase (GM 4.6D) activity;

(e) a nucleotide sequence which encodes a peptide having GM4.6D activity and which hybridizes with the sequence of (a) in either 4×SSC at 65° C. or 50% formamide and 4×SSC at 42° C., and

(f) allelic variants of the nucleotide sequence of SEQ ID NO:1.

2. The polynucleotide of claim 1 comprising the nucleotide sequence of SEQ ID NO:1.

3. The polynucleotide of claim 1 comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:2.

4. The polynucleotide of claim 1 comprising a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:3.

5. An expression vector comprising the polynucleotide of claim 1 and an expression control sequence.

6. A host cell transformed with the vector of claim 5.

7. A process for producing a GM4.6D. said process comprising:

(a) establishing a culture of the host cell of claim 6 in a suitable culture medium; and

(b) isolating said enzyme from said culture.

* * * * *

-continued

(i i) MOLECULE TYPE: oligoucleotide

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CAGAAAGTCC ACTTCAGTCG GTCGGTAGTA 30

What is claimed is:

1. A composition comprising a peptide comprising an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence of SEQ ID NO:2;

(b) the amino acid sequence of SEQ ID NO:3; and

(c) a fragment of the amino acid sequence of (a) or (b) having GM4,6D activity;

said peptide being substantially free from association with other proteins.

2. A pharmaceutical composition comprising the peptide of claim 1 and a pharmaceutically acceptable carrier.

3. The peptide of claim 1 comprising the amino acid sequence of SEQ ID NO:2.

4. The peptide of claim 1 comprising the amino acid sequence of SEQ ID NO:3.

5. A composition comprising a peptide made according to a process comprising:

(1) establishing in a suitable culture medium a culture of a host cell transformed with an expression vector comprising a polynucleotide and an expression control sequence; and

(2) isolating said enzyme from said culture;

wherein said polynucleotide comprises a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence of SEO ID NO:1;

(b) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:2;

(c) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:3;

(d) a nucleotide sequence encoding a fragment of the amino acid sequence of (b) or (c) having GM4,6D activity

(e) a nucleotide sequence which encodes a peptide having GM4,6D activity and which hybridizes with the sequence of (a) in either 4×SSC at 65° C. or 50% formamide and 4×SSC at 42° C.; and

(f) allelic variants of the sequence of (a), (b) or (c).

6. A composition comprising a peptide encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence of SEQ ID NO:1;

(b) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:2;

(c) a nucleotide sequence encoding the amino acid sequence of SEQ ID NO:3;

(d) a nucleotide sequence encoding a fragment of the amino acid sequence of (b) or (c) having GM4,6D activity;

(e) a nucleotide sequence which encodes a peptide having GM4,6D activity and which hybridizes with the sequence of (a) in either 4×SSC at 65° C. or 50% formamide and 4×SSC at 42° C.; and

(f) allelic variants of the sequence of (a), (b) or (c).

7. A method for identifying an inhibitor of GM4,6D activity, said method comprising:

(a) combining a substrate, a candidate inhibitor compound, and the composition of claims 5 or 6; and

(b) observing whether said composition converts said substrate.

* * * * *

1: Arch Biochem Biophys 1986 Sep;249(2):533-45 Related Articles, Link

Two Chinese hamster ovary glycosylation mutants affected in the conversion of GDP-mannose to GDP-fucose.

Ripka J, Adamany A, Stanley P.

A biochemical basis for the pea and lentil lectin resistance of two Chinese hamster ovary (CHO) cell mutants, Lec13 and Lec13A, was investigated. Studies of the G glycopeptides of vesicular stomatitis virus grown in the mutants indicated that Lec13 cells essentially lack the ability to add fucose tc complex carbohydrates while Lec13A cells synthesize significant proportion: of fucosylated, complex moieties. However, both mutants were known to be reverted to lectin sensitivity by growth in L-fucose, making them similar to the mouse lymphoma mutant, PLR1.3, which is defective in the conversion of GDP-mannose to GPD-fucose [M. L. Reitman, I. S. Trowbridge, and S. Kornfeld (1980) J. Biol. Chem. 255, 9900-9906]. Optimal conditions for the production of GDP-fucose from GDP-mannose by CHO cytosol were found to occur at pH 8 in the presence of 7.5 microM GDP-mannose, 15 mM Mg2+, 0.2 mM NAD+, 0.2 mM NADPH, 10 mM niacinamide, 5 mM ATP, and 50 mM Tris-HCl. Under these conditions, Lec13 cytosol produced no detectable GDP-fucose nor GDP-sugar intermediates while Lec13A cytosol produced significant quantities of both. Mixing experiments with Lec13 cytosol identified the first enzyme of the conversion pathway (GDP-mannose 4,6-dehydratase, EC 4.2.1.47) as the site of the block. In addition to being markedly reduced, the Lec13A 4,6-dehydratase activity was relatively insensitive to changes in pH in comparison to the activity in parental cytosol, suggesting that Lec13A cells might possess a structurally altered GDP-mannose 4,6-dehydratase enzyme.

PMID: 2428310 [PubMed - indexed for MEDLINE]

1: Biochem J 1991 Nov 1;279 (Pt 3):801-6

Related Articles, Link

Participation of an endogenous inhibitor of fucosyltransferase activities in the developmental regulation of intestinal fucosylation processes.

Ruggiero-Lopez D, Biol MC, Louisot P, Martin A.

Department of General and Medical Biochemistry, INSERM-CNRS U. 189, France.

During the rat weaning period (about day 19 after birth) the intestinal maturation is accompanied by a drastic increase in the fucose content of mucosal glycoconjugates, concomitant with an increase in fucosyltransferase activities. The regulation of this fucosylation process appears to be a rather complex phenomenon, which involves several systems controlling fucosyltransferase activity or substrate availability. An endogenous protein inhibitor of the fucosyltransferase activities displays an opposite developmental pattern to that of fucosyltransferase activities, since its activity is high before weaning and is decreased 5-fold after weaning. Similarly, the GDP-fucose pyrophosphatase activity markedly decreases at weaning. The transformation of GDP-mannose into GDP-fucose increases early, at day 18, preceding the increase in fucosyltransferase activities. Before weaning, and especially at days 14 and 18, high levels of GDP-4-dehydro-6-deoxymannose, the product of the GDP-mannose 4,6-dehydratase activity, are produced during the transformation of GDP-mannose into GDP-fucose, even in excess of reduced coenzyme. This fact indicates that the second step of the transformation (epimerase-reductase reaction) could be a limiting factor for GDP-fucose availability before weaning, but not after weaning. The inverse relationship between the mucosal fucose content (or the fucosyltransferase activity) and the endogenous protein inhibitor during normal postnatal development supports the hypothesis of a physiological role for this inhibitor.

PMID: 1953674 [PubMed - indexed for MEDLINE]

Display Abstract Show: 20 Sort Send to Text

1: J Biol Chem 1980 Oct 25;255(20):9900-6

Related Articles, Link

Mouse lymphoma cell lines resistant to pea lectin are defective in fucose metabolism.

Reitman ML, Trowbridge IS, Kornfeld S.

Two mutants of the BW5147 mouse lymphoma cell line have been selected for their resistance to the toxic effects of pea lectin. These cell lines, termed PLR1.3 and PHAR1.8 PLR7.2, have a decreased number of high affinity pea lectin-binding sites (Trowbridge, I.S., Hyman, R., Ferson, T., and Mazauskas, C. (1978) Eur. J. Immunol. 8, 716-723). Intact cell labeling experiments using [2-3H]mannose indicated that PLR1.3 cells have a block in the conversion of GDP-[3H]mannose to GDP-[3H]fucose whereas PHAR1.8 PLR7.2 cells appear to be blocked in the transfer of fucose from GDP-[3H]fucose to glycoprotein acceptors. In vitro experiments with extracts of PLR1.3 cells confirmed the failure to convert GDP-mannose to GDP-fucose and indicated that the defect is in GDP-mannose 4,6-dehydratase (EC 4.2.1.47), the first enzyme in the conversion of GDP-mannose to GDP-fucose. The block in the PLR1.3 cells could be bypassed by growing the cells in the presence of fucose, demonstrating that an alternate pathway for the production of GDP-fucose presumably via fucose 1-phosphate is functional in this line. PLR1.3 cells grown in 10 mM fucose showed normal high affinity pea lectin binding. PHRA1.8 PLR7.2 cells synthesize GDP-fucose and have normal or increased levels of GDP-fucose:glycoprotein fucosyltransferase when assayed in vitro. The fucosyltransferases of this clone can utilize its own glycoproteins as fucose acceptors in in vitro assays. These findings indicate that this cell line fails to carry out the fucosyltransferase reaction in vivo despite the fact that it possesses the appropriate nucleotide sugar, glycoprotein acceptors, and fucosyltransferase. The finding of decreased glycoprotein fucose in two independent isolates of pea lectin-resistant cell lines and the restoration of high affinity pea lectin binding to PLR1.3 cells following fucose feeding strongly implicates fucose as a major determinant of pea lectin binding.

PMID: 6159350 [PubMed - indexed for MEDLINE]